

Does the two-week rule pathway improve the diagnosis of soft tissue sarcoma? A retrospective review of referral patterns and outcomes over five years in a regional sarcoma centre

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ABSTRACT

INTRODUCTION The *NHS Cancer Plan* was introduced in 2000 and included guidelines for the rapid assessment and referral of cases of suspected malignancy. We wished to assess the efficiency and appropriateness of patients referred under the Department of Health's general practitioner referral guidelines implemented for sarcomas in December 2000.

PATIENTS AND METHODS A retrospective case-note review was performed of all patients referred to our regional soft tissue sarcoma unit between 1 January 2004 and 31 December 2008. Patients referred under the two-week guidelines and all patients referred routinely were analysed. The main outcome measures were the total number of patients referred on the basis of the two-week guidelines and the proportion they constitute of all referrals. The referring criteria were noted and compared to the observed criteria recorded. The final histological diagnosis of patients referred on the basis of the two-week guidelines are documented.

RESULTS A total of 2746 referrals for suspected sarcoma were made from January 2004 to December 2008. Of these, 154 referrals were made under the two-week rule of which 102 were referred purely on the clinical criteria for suspected soft tissue sarcoma. The remaining patients were referred after non-urgent special investigations indicated the possibility of sarcoma. Twelve patients referred under the two-week rule were proved to have sarcoma, nine after specific investigations including imaging or histological diagnosis. Of the 102 patients referred on clinical suspicion of a sarcoma, two patients had proven soft tissue sarcomas and one patient a cutaneous sarcoma. Between 2004 and 2008, the number of 2-week referrals rose 25-fold but accounted for an increase of less than 1% of the sarcomas treated in this unit.

CONCLUSIONS The numbers of all referrals for suspected sarcoma are increasing; however, the rate of increase of 2-week referrals is increasing faster than routine referrals and will exceed it in 2012 if current trends continue. There has not been a commensurate rise in the detection of sarcoma or, more specifically, diagnosis of the deep sarcomas associated with worse prognosis. Current clinical guidelines have essentially had no impact on the early diagnosis and treatment of soft tissue sarcoma, and may negatively impact on the treatment of patients with proven sarcoma by delaying treatment within a regional centre because of redirection of a large number of patients with benign abnormalities to such centres.

KEYWORDS

Two-week rule – Soft tissue sarcoma

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Adult soft tissue sarcomas are rare tumours, with incidence of around 4 per 100,000 population per year in Europe¹ and 1000 new cases per annum in the UK.² Of these, 60% will arise in the extremities, so making them accessible to clinical examination.³ Despite various referral guidelines having been instituted, considerable delays can occur which may adversely affect management and prognosis. Clark *et al.*⁴ suggested that a fifth of patients with soft tissue sarcomas

encountered important delays in referral to a specialist unit. This delay was thought likely to have a detrimental effect on treatment options and outcomes, including survival in some patients. Medical professionals rather than patients contribute the greatest source of delay in patients reaching a specialist centre for treatment of soft tissue sarcoma.⁵

The *NHS Cancer Plan* was published in 2000.² This document detailed the UK Government's comprehensive

national programme for investment in, and reform of, cancer services in the NHS. Included in these reforms has been a drive to reduce the waiting time of cancer patients from referral to diagnosis and treatment. The clinical features that are stipulated in the referral guidelines to be suggestive of malignancy in a soft tissue mass are: size above 5 cm, painful, an increase in size, lesion positioned deep to fascia and a recurrent mass. As a way of overcoming the adverse outcomes associated with delayed presentation of a malignancy, the Government White Paper,⁶ *The New NHS – Modern, Dependable*, stated that all patients with a suspected cancer would be able to see a specialist within 2 weeks of their GP deciding that they should be seen urgently. This standard was implemented for sarcomas in December 2000. The criteria listed above form the basis of an urgent referral for suspected soft tissue sarcoma. Similar strategies have been adopted in other malignancies, and recent published reviews of workload changes and outcome data relating to the 2-week wait criteria of these cancers have shown a wide range of diagnostic efficiency. In breast cancer, approximately 10–20% of these urgent referrals are shown to have malignancy,^{7–9} with a similar rate of 10% for colorectal cancer.^{10,11} Some authors have indicated a decrease in ‘standard’ referrals since the introduction of the system, with a commensurate rise in urgent referrals, which has necessitated a shift in practice towards making more clinical appointments available for suspected cancer referrals at the expense of routine work. This is concerning since the rate of cancer detection in non-urgent referrals has doubled over the same time period.⁷

The *Improving Outcomes Guidance for Sarcoma* states that ‘only one in ten referrals of ‘suspicious lumps’ will be a sarcoma’.¹² However, there is no supporting data for this assumption either in this document or the supporting National Institute for Health and Clinical Excellence (NICE) guidelines *Referral Guidelines for Suspected Cancer*.¹⁵ Given that the diagnostic rate of breast and colorectal cancer for 2-week referrals is approximately 10% and these malignancies are many times more common than sarcoma, it seems likely that a diagnostic pick-up rate of 10% for sarcoma is a considerable overestimate.

This paper aims accurately to identify the true diagnostic rate for patients with sarcoma in the cohort of patients referred from primary care on a two-week rule basis according to the clinical guidelines for an urgent referral of suspected soft tissue sarcoma. It also analyses the changes in referral demographics over a 5-year period since the publication of *Improving Outcomes Guidance for Sarcoma*, and evaluates the impact of the urgent referral pathway on the stated aim to decrease delays in presentation of soft-tissue sarcoma. The implications for service in a regional sarcoma centre are discussed.

Patients and Methods

Since the introduction of the two-week rule, the Royal

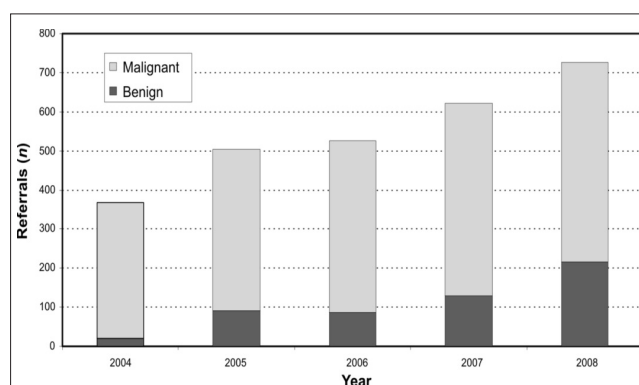


Figure 1 Total referrals to Royal Marsden Hospital soft tissue sarcoma unit per year.

Marsden Sarcoma Unit has kept a prospective database of these referrals. This database was searched to identify all relevant patients referred between 1 January 2004 and 31 December 2008. Their electronic patient records and referral pathways were reviewed, with reference to the clinical diagnostic criteria present and any imaging or pathology available at referral. These findings were compared to those of the consultant at the patient's first clinic appointment. All final histology reports were obtained from the electronic patient record. The total number of referrals to the unit and their diagnosis during this period was obtained from a second prospective database based on MDT data, which included all urgent and standard referrals.

Results

A total of 2746 referrals for suspected sarcoma were made to the unit from January 2004 to December 2008. Of these, 154 referrals were made under the two-week rule; the remaining 2592 referrals were received after non-urgent referral locally had resulted in a histological (post-excision/biopsy) or imaging investigation suggesting a sarcoma diagnosis. Of these patients, 102 were referred purely on the clinical criteria for suspected soft tissue sarcoma. The remaining 52 were referred to the unit: (i) after imaging indicated the possibility of a soft tissue malignancy; (ii) because the patient was known to have a sarcoma and the general practitioner was concerned about a local recurrence; or (iii) in a small number of cases, because a small cutaneous sarcoma was excised inadvertently under the care of a general practitioner.

Of the 102 referrals on clinical criteria alone, only two patients (2%) were eventually diagnosed with a soft tissue sarcoma, although a number of patients were diagnosed with other malignancies or fibromatosis and, therefore, subsequently underwent treatment. The first was a 4-cm myxoid liposarcoma lying in the subcutaneous tissues of the

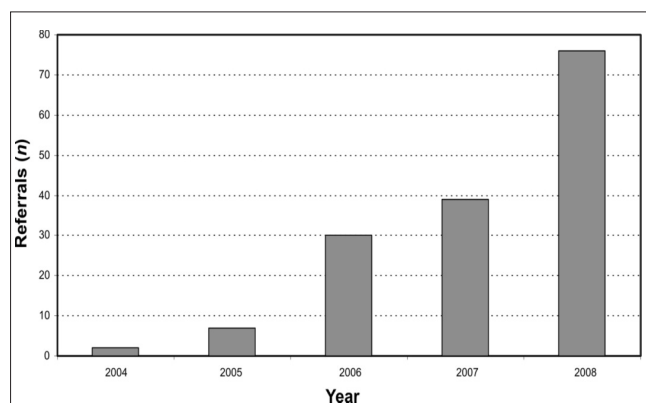


Figure 2 Two-week rule referrals to Royal Marsden Hospital soft tissue sarcoma unit per year.

inner thigh and the second a 3-cm, low-grade, spindle cell sarcoma arising in the subcutaneous tissues over gluteus maximus. (A third patient was diagnosed with a low-grade cutaneous sarcoma, dermatofibrosarcoma protruberans [DFSP], but this arose in the skin and not the soft tissue.) The diagnoses for the non-sarcoma group are shown in Table 1.

Of the 52 patients referred after imaging, possible recurrence or excision rather than on clinical grounds alone, nine patients were eventually shown to have a diagnosis of soft tissue sarcoma. Three patients were referred urgently for further management after an inadvertent excision biopsy in primary care revealed the diagnosis of sarcoma. Three patients had undergone some form of imaging arranged in primary care on a non-urgent basis (MRI in two cases and CT in one case) that strongly suggested the diagnosis of sarcoma and advised tertiary referral. Finally, three patients with previously known sarcomas who were already under follow-up developed a local recurrence at the site of their primary tumour and were referred urgently for management of the recurrence.

Figure 1 shows the trend for increasing referrals for all patients referred to this regional sarcoma unit over the 5-year study period with the number of referrals subdivided by the eventual diagnosis of benign or malignant disease. Figure 2 shows the increase in the number of patients referred directly from primary care under the two-week rule over the same period. The proportion of patients with eventual benign diagnosis has increased from approximately 20% in 2004 to nearer 30% in 2008. This increase is accounted for entirely by the increase seen in patients with benign disease referred on the basis of an urgent suspected sarcoma.

The pattern of referrals in this regional sarcoma unit in 2008 (subdivided by benign or malignant diagnosis) is shown in Figure 3. While the proportion of 2-week referrals remains small, at 10.5%, the rate of increase in this type of

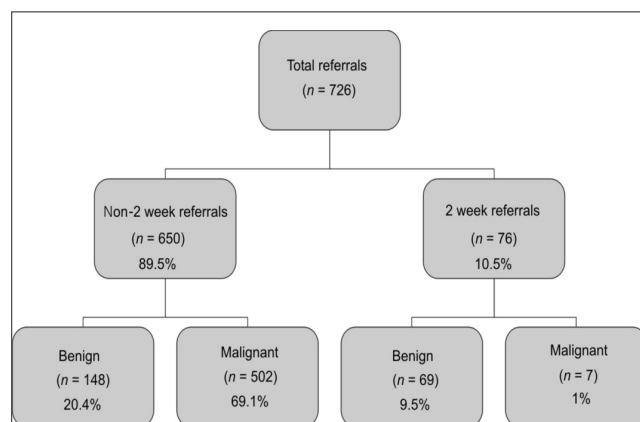


Figure 3 Schematic diagram of unit workload January–December 2008. Percentage figures are of total unit case number. The percentage of new sarcoma diagnoses on the basis of the clinical criteria on 2-week referrals was 0.2% of all patients seen in 2008.

Table 1 Summary of non-sarcoma diagnoses in patients referred directly from primary care on a two-week rule basis

Diagnosis	Cases (n)
Lipoma	52
No lesion/abnormality found	26
Inflammatory change	14
Arteriovenous malformation	7
Chronic haematoma	7
Schwannoma	6
Fibromatosis	4
Fat necrosis	3
Myxoma	3
Sebaceous cyst	3
Baker's cyst	2
Giant cell tumour	2
Infective lymphadenopathy	2
Osteoarthritis	2
Other metastatic malignancy*	2
Fibrous histiocytoma	1
Granulomatous panniculitis	1
Keratoacanthoma	1
Lymphoma	1
Neuroma	1
Solitary fibrous tumour	1
Tuberculous lesion	1
Total	142

*Only two of 142 patients with non-sarcoma diagnoses proved to have another malignant diagnosis, which were soft tissue deposits from a breast cancer and a gynaecological cancer.

Table 2 Summary of referred and observed criteria

Suspected sarcoma criteria	Criteria used in referral	Criteria observed
> 5 cm in size	92	61
Rapid increase in size	90	50
Deep to fascia/fixed/immobile	69	39
Painful	20	8
Recurrent lesion	8	8

referral has been substantial over the last 5 years. If this trend continues, by 2012 the majority of patients referred to this regional centre would be from primary care, and yet the number of *de novo* sarcoma diagnoses treated would rise by less than 1%.

There were marked discrepancies noted between the clinical criteria that the patient had been referred with, compared to the observed criteria at the regional sarcoma centre where the patient had been seen by a sarcoma specialist (Table 2). Three patients were referred in on an urgent basis, despite having none of the referral criteria.

Discussion

This study attempted to evaluate two issues. First, whether the development of the two-week rule criteria for urgent suspected sarcoma referrals in primary care had indeed resulted in improved diagnosis of poor-prognosis, deep sarcomas at an earlier stage. Second, the service implications for a national treatment centre for sarcoma as a result of the development and implementation of these referral guidelines.

The first finding is that the number of cases of soft tissue sarcoma that were diagnosed on the basis of clinical criteria alone was very low at below 2%. Furthermore, these were superficial subcutaneous or cutaneous sarcomas, that carry a good prognosis and can be managed by simple surgical excision, rather than deep-seated sarcomas that currently account for the poor outcome in sarcoma.¹⁴ Although a number of other lesions requiring treatment were also diagnosed, these were not in the target group for which the *Improving Outcomes Guidance for Sarcoma* guidance was intended to improve outcome. Hence, not only are the actual number of new sarcoma diagnoses seen as a result of these guidelines very small, but it is unlikely that they would impact on outcome as a poor prognosis is strongly related to a deep location. It is of concern that, despite significant investment in cancer services concomitant with the *NHS Cancer Plan*, and the IOG's stated aim of reducing these delays, none of the sarcomas diagnosed in the urgent

referral cohort were in this poor prognostic group. All poor-prognosis sarcomas seen by this unit were referred outside the 2-week pathway.

The second major finding of this paper relates to the service implications for sarcoma treatment centres. The number of two-week rule referrals has increased 25-fold in a 4-year period in our unit, while the proportion of sarcomas treated has changed by less than 0.3% as a result of this increase in referral from primary care. Of the cohort of patients who are referred to this unit after investigation at another institution, the percentage of patients with a soft tissue malignancy is 77%. While in 2005–2006 the number of patients referred direct from primary care to this institution was 1% of approximately 500 new referrals, at the current rate of increase the number of referrals from primary care would overtake the secondary referrals in 2012 but the number of new sarcomas diagnosed would increase by less than 1%.

Enzinger and Weiss¹⁵ suggested that, for every malignant soft tissue tumour of any type examined by a pathologist, there are at least 100 benign soft tissue tumours. The incidence of benign soft tissue tumours is about 300 per 100,000 population.¹⁶ In an average general practice of 3000 patients, at least three cases of benign soft tissue tumour per year may be expected. However, only one case of soft tissue sarcoma would be expected in this population every 24 years.¹⁷

It is well-recognised, however, that soft tissue sarcomas present late with the average size of presentation of a deep extremity sarcoma being 8 cm and that of a superficial sarcoma being 3 cm.^{5,18} The reason for late presentation is not entirely understood but is partly because many of these sarcomas will have no symptoms other than the presence of a painless mass. Many sarcomas, especially those associated with a poor prognosis, arise in deep-seated anatomical locations such as the retroperitoneum or proximal extremity muscle groups. Delays mostly occur prior to referral to a treatment centre.⁴ It is of note that the two superficial sarcomas diagnosed on clinical grounds in the present series were around the reported median size at presentation for superficial tumours.

One facet of the *Improving Outcome Guidelines for Sarcoma*¹² focused on development of early diagnostic criteria for soft tissue sarcoma and early referral on a two-week rule basis for use in primary care, even though it had previously shown that actual incidence of these tumours in individual GP practices is extremely low.

Such early referral criteria had been developed for other tumour types (especially breast and colorectal) such that, in breast cancer practice, most patients are now referred on the basis of an urgent suspected cancer on a two-week rule basis.^{7–11} However, for common tumours, the incidence within primary care is reasonably high so there is an *a priori* reason to assume that urgent referrals will result in a diagnosis of malignancy in a significant proportion of cases.

Furthermore, referrals will be to the local unit and treatment of both benign and malignant diagnoses will be in that unit. This is in sharp contrast to rare malignancies where the treatment of the condition when diagnosed will be centralised nationally into a small number of high-volume centres. While the *Improving Outcome Guidelines for Sarcoma* has suggested that there would be a series of diagnostic clinics that exist separately from a treatment centre, perhaps in each cancer network, at this point in time, 10 years after the introduction of the IOG guidelines, the reality is that most cancer networks have no such arrangement. Many networks intend to fulfil their diagnostic requirements for sarcoma peer review by utilising the diagnostic facilities in the treatment centre. Therefore, there are a huge number of cases now referred directly from primary care to a sarcoma treatment centre that may be many miles away. In the current series, we have not sought to undermine the urgent referral principle; earlier diagnosis will undoubtedly be of benefit to sarcoma patients. Rather, we aimed to evaluate the service impact resultant from the introduction of these guidelines.

Recent reports have suggested that ultrasound can be an effective intermediary triage stage prior to any patient being seen in a sarcoma treatment centre.¹⁹ More prospective studies of the impact of such a strategy would be welcome; although ultrasound is not the best diagnostic modality in soft tissue sarcoma, it would be highly effective at triaging two major patient groups shown in Table 1 – those with no soft tissue abnormality and those with cutaneous lipomas. This accounts for over 50% of referrals. If this were coupled with a local core biopsy service the number of non-sarcoma diagnoses reached prior to referral to the specialist centre would be very much higher.

Conclusions

This study has demonstrated that the current clinical guidelines have had essentially no impact upon the early diagnosis and treatment of sarcoma from primary care, particularly those patients with poor-prognosis tumours, and may impact negatively on the treatment of patients with sarcoma by delaying treatment within a treatment centre because of a new and potentially overwhelming benign diagnostic workload of non-malignant abnormalities. We would, therefore, recommend that no patient should be referred to a sarcoma treatment centre from primary care without an initial screening ultrasound scan that suggested the possibility of an soft tissue sarcoma. We believe that all cancer networks should provide this service locally to minimise excessive travel and patient anxiety when those with benign or no abnormalities are urgently referred to a regional cancer centre.

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